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# Oxytocin reduces interpersonal distance: Examining moderating effects of childrearing experiences and interpersonal context in virtual reality

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## ABSTRACT

Oxytocin has been shown to stimulate social approach behaviors, although effects may depend on contextual and individual difference factors. Here, we examined intranasal oxytocin effects on interpersonal distance using an immersive Virtual Reality paradigm, taking into account early caregiving experiences and interpersonal context as potential moderators. Participants were 180 women who received 24 IU oxytocin or a placebo and had reported how often their mother used love withdrawal as a disciplinary strategy, involving withholding love and affection after a failure or misbehavior. We used a virtual stop-distance paradigm, instructing participants to approach a virtual person or to stop an approaching virtual person at a preferred distance (passive approach). In order to examine the role of interpersonal context in shaping oxytocin effects, facial expressions and bodily gestures of the virtual person were manipulated. The person showed a dynamical expression of sadness, happiness, anger, fear, disgust, or no emotional expression in six different emotion conditions. We found that oxytocin reduced interpersonal distance across the different emotion conditions, but only in individuals with lower levels of love withdrawal. In addition, oxytocin reduced anxiety levels during passive approach, in particular in the disgust condition, but only in individuals with lower levels of maternal disciplinary love withdrawal. Individuals with more love withdrawal experienced more anxiety while being approached by a virtual person displaying disgust or fear, but benefitted less from anxiety-reducing oxytocin effects. These results are consistent with previous research showing a dysregulated oxytocinergic system after childhood adversity and indicate that oxytocin may be less effective for individuals who are most in need of an intervention because of a problematic family background.

## 1. Introduction

Interpersonal distance is the space we choose to maintain with other people. It is considered a form of nonverbal communication that plays an important role in social interactions and varies depending on individual preferences (Iachini et al., 2016), contexts (Scheele et al., 2012), and the familiarity of the person with whom the space is shared. For example, we choose to maintain a greater distance to strangers than close friends (Güroğlu et al., 2008), suggesting that interpersonal distance is an indicator of affiliation and emotional closeness. Interpersonal distance has also been interpreted as a tendency to either approach or avoid social stimuli (Cohen and Shamay-Tsoory, 2018), related to affective needs and boundaries (Bekker et al., 2016). It is often examined with stop-distance paradigms, in which the participant

is either asked to stop an approaching person at a preferred distance or is asked to control the size of their interpersonal space by actively approaching the other person and choosing themselves when to stop.

Previous studies have explored neurobiological mechanisms underlying individual differences in interpersonal distance and point to a role of the neuropeptide oxytocin in regulating social approach (Cohen et al., 2017). Oxytocin is involved in a range of social behaviors and has been shown to stimulate trust (Van IJzendoorn and Bakermans-Kranenburg, 2012), in-group altruism (De Dreu et al., 2010), empathy (Shamay-Tsoory et al., 2013), and emotion recognition (Shahrestani et al., 2013). One hypothesis that has been proposed to explain these general social effects is the social approach/withdrawal hypothesis of oxytocin, which states that oxytocin increases social approach behaviors and decreases withdrawal behaviors (Harari-Dahan and Bernstein,

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2014, 2017; Piva and Chang, 2018). However, with respect to interpersonal distance, conflicting results have been found, with oxytocin inducing either closeness or separation. For example, Scheele et al. (2012) showed that intranasal administration of oxytocin resulted in a greater distance between men in a monogamous relationship and an attractive woman. Similarly, Cohen et al. (2017) showed that intranasal oxytocin increased interpersonal distance in a paradigm with approaching protagonists, in particular to strangers. In contrast, oxytocin increased social approach behaviors in a paradigm in which participants actively exerted control over their space and were instructed to actively approach the other person (Cohen and Shamay-Tsoory, 2018).

One explanation that has been proposed for these seemingly contrasting findings is that stop-distance paradigms that contain approaching figures may provoke threat from personal space intrusion (Cohen et al., 2018). In the context of threat, oxytocin may induce a tendency to separation and increase social space, whereas it may stimulate a tendency to closeness in the absence of threat. Indeed, contextual factors have been shown to moderate and shape the direction of the effects of oxytocin on social behavior (Bartz et al., 2011). More specifically, oxytocin stimulates trust and altruistic behaviors towards in-group members or in safe social situations, but at the same time increases antisocial behaviors towards threatening out-group members and in hostile contexts (De Dreu, 2012). These paradoxical effects may be explained by another prominent hypothesis for oxytocin effects on social behavior: The social salience hypothesis, which states that oxytocin increases sensitivity to social cues of safety and threat (Shamay-Tsoory and Abu-Akel, 2016). This general effect of increased salience of contextual cues has been proposed to underlie the paradoxical effects of oxytocin, with increased approach and affiliative responses in safe situations but more avoidant or defensive responses in the presence of threat.

In addition to contextual factors, individual difference factors have also been shown to moderate the effects of oxytocin (Bartz et al., 2011). More specifically, studies point to a moderating role of early childhood experiences on the prosocial effects of intranasal oxytocin and indicate that individuals with negative childhood experiences show reduced sensitivity to oxytocin (Bakermans-Kranenburg and Van IJzendoorn, 2013). For example, oxytocin has stress-reducing effects, as reflected by cortisol decreases after social stress, but these effects are impeded in individuals with a history of early parental separation (Meinlschmidt and Heim, 2007). Similarly, in several previous studies, we showed that oxytocin effects on social behavior are absent in individuals with experiences of maternal use of love withdrawal (Riem et al., 2013a), a disciplinary strategy that involves withholding love and affection when a child misbehaves. Parental use of love withdrawal has been associated with negative child outcomes, including fear of failure (Huffmeijer et al., 2013), and it is considered emotional maltreatment when it is used excessively (Euser et al., 2010).

In the current study, we examined intranasal oxytocin effects on interpersonal distance, taking into account both contextual and individual difference moderators. We used a newly developed immersive Virtual Reality (VR) paradigm (Steenbakkers et al., 2019), in which female participants were instructed to either approach a virtual person with different emotional expressions or to stop an approaching virtual person at their preferred distance. In order to examine the role of interpersonal context in shaping oxytocin effects, we manipulated the facial expression of the virtual person and we devised the VR paradigm so that the virtual person showed a dynamical bodily and facial expression of sadness, happiness, anger, fear, disgust, or no emotional expression in different emotion conditions. Two contrasting predictions can be made regarding how oxytocin will affect distance in these socially varying contexts. 1). According to the approach/withdrawal hypothesis, oxytocin would stimulate approach behaviors in positively-valenced interactions and would reduce withdrawal behaviors in negatively-valenced interactions, possibly through anxiety reduction (Piva and Chang, 2018). This would result in reduced interpersonal

distance in both negatively-valenced and positively-valenced interactions. 2). In contrast, according to the social salience hypothesis, oxytocin would enhance the salience of social cues, and, as a result, would lead to opposing effects during interactions signalling threat versus safety. Thus, oxytocin would stimulate sensitivity to the emotional expressions, would enhance prosocial approach behaviors towards a person displaying sad or happy facial expressions (signalling safety and absence of threat), but would increase distance from a person displaying angry, fearful, or disgusted facial expressions (signalling potential threat or rejection). In addition, we examined the role of maternal use of love withdrawal in shaping oxytocin effects and regulating interpersonal distance. Consistent with previous studies, we expected that oxytocin effects would be less pronounced in individuals with more experiences of love withdrawal.

## 2. Materials and methods

### 2.1. Participants

The sample consisted of 180 female undergraduate students from Tilburg University. The ages ranged from 18 to 27 years old ( $M = 20.12$ ,  $SD = 1.78$ ). The majority of participants were born in the Netherlands (48.9%), Germany (28.9%), or another European country (20.6%) and did not have prior experience with virtual reality (86.7%). Of all participants 56.7% used hormonal contraceptives. Exclusion criteria involved drug or alcohol abuse, nasal problems, use of prescribed medication (except contraception), psychiatric and neurological disorders, cardiovascular diseases, and a high blood pressure. Further, participants who were pregnant, breastfed or had children were excluded from this study. Participants were randomly assigned to the oxytocin or the placebo condition ( $N = 90$  oxytocin,  $N = 90$  placebo). Sample size was based on an a priori power analysis using G\*Power 3.1 for repeated measures (within-between interactions), which showed that a sample size of 166 is sufficient to detect small effects ( $f = .10$ ,  $\alpha = .05$ , power .95, 6 measurements, 2 groups). Oversampling was done in order to be able to test moderation effects of love withdrawal. Participants received a monetary reward or study credits for participation. Permission for this study was obtained from the Medical Ethics Committee Brabant (NL60593.028.17) and all participants gave informed consent. The study was registered in the Dutch Trial Register (NTR6513).

### 2.2. Procedure

Participants were asked to complete questionnaires on childhood experiences approximately one week before a lab session. They were invited for the lab session, preferably in the luteal phase of their menstrual cycle in order to control for influences of menstrual cycle. During the luteal phase, plasma oxytocin levels are lower (Salonia et al., 2005) and more responsive to stimulation such as by nipple stimulation (Leake et al., 1984). Women were asked about the date of their last menstruation and this information was used to schedule the lab session. Menstrual phase and hormonal contraceptives were balanced across the placebo and oxytocin group: 12 participants in the oxytocin and 11 participants in the placebo group were in the follicular phase, whereas 79 participants in the oxytocin group and 78 participants in the placebo group were in the luteal phase. In the placebo group, 57 participants used hormonal contraceptives, and in the oxytocin group, 45 participants used hormonal contraceptives. They were instructed to abstain from alcohol during the 24 h before the start of study, and from caffeine and smoking on the data collection day. At the start of the lab session, participants took 6 puffs of nasal spray containing oxytocin (24 IU total) or 6 puffs of a placebo spray under supervision of the experimenter. Drug administration was double-blind. Participants started with practice trials of the virtual interpersonal distance paradigm approximately 15 min after nasal spray administration. The actual paradigm was

administered approximately 20 min after administration. Previous studies have shown intranasal oxytocin effects after similar waiting time (MacDonald et al., 2011).

### 2.3. Virtual interpersonal distance paradigm

We used a newly developed interpersonal distance Virtual Reality (VR) paradigm, developed in collaboration with the DAF Technology Lab, Tilburg University (Steenbakkers et al., 2019), based on the Distance-Closeness paradigm described by Bekker et al. (2016). This VR paradigm permits participants to control the interpersonal distance between a virtual person (avatar) of the same sex and themselves, using a control-box (held-hand single button operated with a thumb) in a three-dimensional computer-generated environment. It enables accurate measurement of approach behaviors and optimal control over experimental conditions in an immersive dynamically adaptable real-life setting.

#### 2.3.1. Adaptations to the interpersonal distance paradigm and used equipment

The paradigm was adapted for the current study and administered in the Behavioral Physiology lab (GO-LAB), Tilburg University, using the Oculus Rift DK2 VR-setup. This setup consists of VR-Glasses and sensors monitoring head orientation. The virtual environment was a square room with a same sex avatar (female) standing in front of the participant (see Fig. 1). The participant and the avatar were positioned on a diagonal line in the virtual room. The virtual setting was created and adapted in Unity. The avatars were purchased online through the unity asset store (<https://www.assetstore.unity3d.com/en#!/content/1760>). Facial expressions of the avatars were also adapted for the study using Unity.

The Spielberger Trait State Anxiety Inventory (STAI) short form (6 items, Marteau and Bekker, 1992; Cronbach's alpha = .71,  $M = 1.78$ ,  $SD = .48$ , range 1–5) was embedded within the virtual task for the measurement of state anxiety. The questions were presented on a virtual wall in the virtual setting. The participants were instructed to select an answer on a virtual wall with a hovering pointer controlled by head movement measured by the Oculus Rift DK2 setup.

#### 2.3.2. Virtual procedure

Before the start of the task, participants were familiarized with an immersive VR with several practice trials to rule out any effects on

anxiety levels due to wow-effects due to inexperience with immersive VR. During the practice trials participants were asked to indicate a preferred position of a neutral “pill”-shaped object. The practice trials were followed by a baseline measurement of state anxiety using the Dutch or English version of the STAI.

The Virtual Interpersonal Distance paradigm started after the baseline anxiety assessment. At the start of each trial, the distance between the avatar and the participant was an equivalent of 3.5 virtual meters. The task consisted of two blocks. In the first block, the participant is approached by an avatar and is asked to stop the avatar at a preferred distance by using the control box. Participants were instructed to stop the walking avatar when they started feeling slightly uncomfortable. In the second block, the participant was instructed to walk towards the avatar in the virtual environment by using the control box and to stop at her preferred distance.

In adaptation to the Virtual Interpersonal Distance Paradigm, the current study used different facial expressions and bodily gestures for the avatar other than neutral. In both blocks, the emotional facial expression and the bodily gestures of the avatar were neutral at the start of each trial, but changed into angry, sad, fearful, disgusted, or happy in different emotion conditions, or remained neutral in a control condition (see supplemental material for a video fragment of the task). The avatar started expressing the emotions and after a few seconds, she walked towards the participant while dynamically expressing an emotion (or without expressing emotion in the neutral condition). Similarly, the avatar kept dynamically displaying the emotion during the entire trial in the condition in which the participant walked towards the person. After each trial, participants rated how angry, sad, happy, disgusted, or anxious the avatar appeared in each condition. This was rated on a five-point Likert scale from 1 (“not at all”) to 5 (“very much”). In addition, state anxiety was measured after each trial. The maximum amount of time of each trial was 10 s. The order of emotion conditions was random and each emotion condition was administered once. A pilot study with 13 undergraduate students showed that the emotions of the avatar were correctly recognized (see Supplemental Material).

### 2.4. Maternal disciplinary use of love withdrawal

The 11-item questionnaire on maternal use of love withdrawal contained seven items of the Withdrawal of Relations subscale of the Children's Report of Parental Behavior Inventory (CRPBI; (Beyers and Goossens, 2003)) and four items from the Parental Discipline

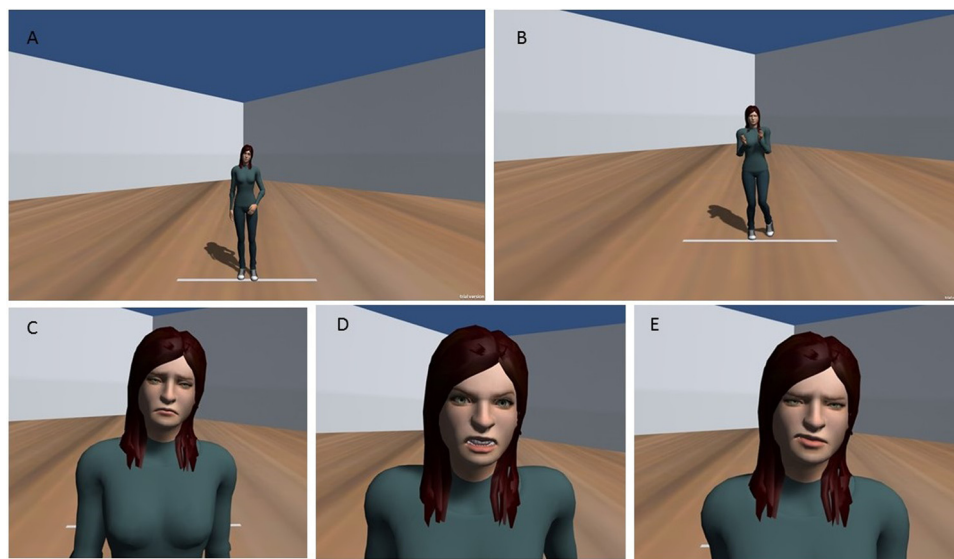


Fig. 1. Virtual Interpersonal Distance Paradigm in the happy condition (A, start of the trial) and fear condition (B, start of the trial), the sad (C), angry (D), and disgust condition (E).

Questionnaire (Hoffman and Saltzstein, 1967), and has been used in previous research (Huffmeijer et al., 2013, 2014; Riem et al., 2014, 2017). Because it is in particular the use of maternal love withdrawal that has been related to low emotional well-being in adolescence and adulthood (Elliot and Thrash, 2004; Renk et al., 2006), we focused on maternal behavior only. The questionnaire was completed online during the first phase of the study. Participants rated how well each of the 11 statements described their mother (e.g., “My mother is a person who, when I disappoint her, tells me how sad I make her”) on a 5-point scale ranging from 1 (not at all) to 5 (very well). Reliability in our sample was .84. Mean total score was 2.30 ( $SD = 0.82$ , range of 1–4.36). The scores did not differ for participants in the oxytocin or placebo condition,  $t(178) = -0.64$ ,  $p = .52$ . Scores were normally distributed.

### 2.5. Data analyses

Anxiety scores and distances were inspected for outliers. Outliers ( $N = 1$  for anxiety in the happy virtual person participant moves condition,  $N = 1$  happy virtual person moves condition) were replaced with the maximum value. Correlations were calculated between love withdrawal and the ratings of the emotions corresponding to the facial expression of the avatar (i.e. sadness rating of the sad female avatar). As previous research has shown that oxytocin affects perception of emotions (Shahrestani, Kemp, & Guastella, 2013), analyses of variance (ANOVA) were performed to test whether oxytocin affected the emotion ratings of the facial expressions. The emotion ratings corresponding to the facial expression of the virtual person (averaged for the ‘approaching participant’ and ‘approaching virtual person’ block) were entered as dependent variable, and treatment group (oxytocin/placebo) was entered as between-subject factor. In order to examine effects of oxytocin, repeated measures ANOVA’s were conducted with anxiety and distance as dependent variables, treatment group (oxytocin/placebo) as between subject factor, and emotion (anger, fear, sadness, happiness, disgust, neutral) as within-subject factor. Analyses were performed separately for the ‘approaching participant’ and ‘approaching virtual person’ block. Distance in the ‘approaching participant’ and ‘approaching virtual person’ block were significantly correlated (neutral condition:  $r = .40$ ,  $p < .001$ ), but were analysed separately because passive approach may be more threatening to participants than active approach. Maternal love withdrawal (continuous), hormonal contraceptives, and menstrual phase were included as covariates in all analyses. STAI state anxiety at baseline was entered as an additional covariate in the analyses with anxiety as dependent variable. Country or origin was initially included as a covariate, but did not significantly affect anxiety or distance and was therefore excluded from the analyses. Excluding country of origin did not change the results.

## 3. Results

### 3.1. Emotional expressions

Table S3 shows that participants rated the emotions that corresponded to the emotional facial expression of the avatar highest, indicating that the emotions of the virtual person were correctly recognized. Oxytocin did not significantly affect the ratings of the facial expressions ( $ps > .19$ ). Correlational analyses showed that maternal love withdrawal was significantly and negatively related to the angry ratings of the angry virtual persons, indicating that individuals with more love withdrawal rated the angry person as less angry (see Table 1).

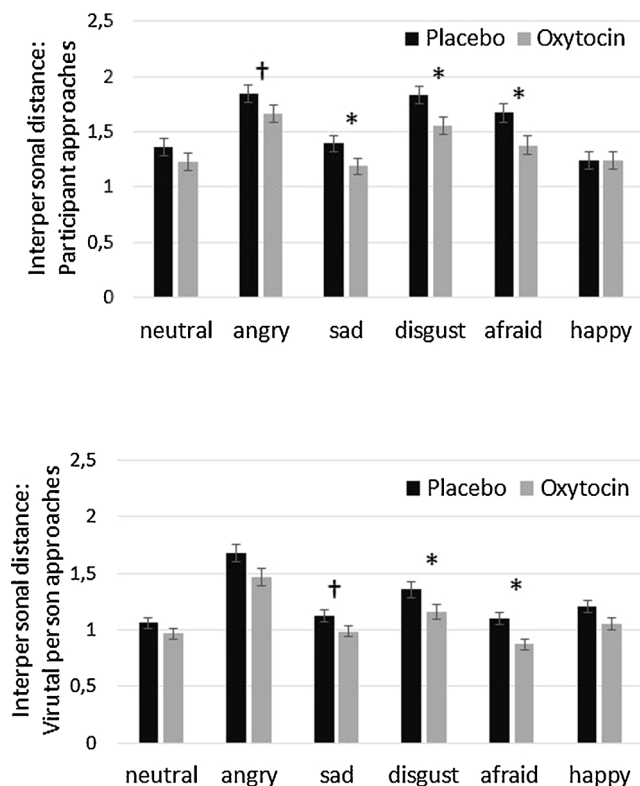
#### 3.1.1. Distance: passive approach

The repeated measures ANOVA showed that oxytocin significantly reduced interpersonal distance when the participant was approached by the virtual person ( $F(1,174) = 7.71$ ,  $p = .006$ , partial  $\eta^2 = .04$ ). In

**Table 1**

Correlations between love withdrawal and the emotion ratings that corresponded to the emotional expression of the virtual person. \*  $p < .05$ .

	Anger	Happy	Afraid	Disgust	Sad	Baseline anxiety
Love withdrawal	-.18*	-.07	.12	.11	.01	0.01



**Fig. 2.** Mean distance (virtual meters) for individuals in the placebo and oxytocin group across the different emotion conditions in the participant approaches block and the virtual person approaches block. \* $p < .05$ , †  $p < .1$ .

**Table 2**

Mean and SD of interpersonal distance and anxiety across the emotion conditions.

	Distance				Anxiety			
	Virtual person approaches		Participant approaches		Virtual person approaches		Participant approaches	
	M	SD	M	SD	M	SD	M	SD
<b>Placebo</b>								
Neutral	1.05	0.46	1.34	0.66	1.82	0.50	1.82	0.49
Angry	1.66	0.73	1.82	0.67	2.31	0.70	2.40	0.74
Sad	1.12	0.50	1.38	0.67	2.03	0.63	2.06	0.58
Disgust	1.35	0.67	1.82	0.76	2.16	0.66	2.22	0.68
Happy	1.10	0.51	1.25	0.58	1.71	0.46	1.59	0.44
Afraid	1.21	0.55	1.66	0.71	1.95	0.57	2.16	0.69
<b>Oxytocin</b>								
Neutral	0.97	0.46	1.26	0.83	1.84	0.53	1.75	0.51
Angry	1.49	0.73	1.70	0.88	2.32	0.74	2.33	0.75
Sad	0.99	0.45	1.20	0.73	2.00	0.54	2.00	0.53
Disgust	1.16	0.58	1.57	0.82	2.10	0.62	2.15	0.65
Happy	0.88	0.39	1.24	0.83	1.68	0.43	1.62	0.44
Afraid	1.06	0.49	1.39	0.80	1.98	0.58	2.03	0.59

addition, there was a significant effect of emotional expression of the virtual person ( $F(3,50, 609.13) = 6.03$ ,  $p < .001$ , partial  $\eta^2 = .03$ ). Fig. 2 and Table 2 present the mean distances across the different



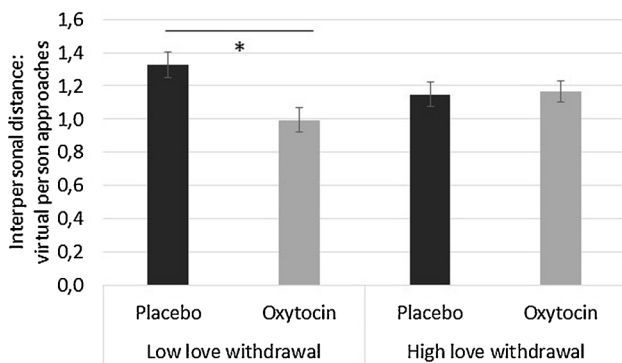


Fig. 3. Mean distance (virtual meters averaged across the different emotion conditions) in the placebo and oxytocin group for individuals with low and high love withdrawal. \*  $p < .05$ .

emotion conditions and indicate smaller distances in the sad, happy, and neutral condition, and larger distances in the angry condition. However, there was no significant effect of love withdrawal on interpersonal distance ( $F(1,174) = 0.01, p = .931$ , partial  $\eta^2 = .00$ ) and no significant interaction between treatment group and emotional expression ( $F(3.50, 609.13) = 1.32, p = .265$ , partial  $\eta^2 = .01$ ). Further, we found a significant interaction between love withdrawal and treatment group ( $F(1,174) = 4.78, p = .030$ , partial  $\eta^2 = .03$ ). Maternal love withdrawal was dichotomized into low and high love withdrawal using a median split (median = 2.18) in order to explore the interaction. Planned contrasts with mean interpersonal distance across the emotion conditions showed that oxytocin reduced interpersonal distance, but only for participants with lower levels of love withdrawal (placebo:  $N = 50, M = 1.33, SD = 0.53$ , oxytocin:  $N = 38, M = 0.99, SD = 0.45$ ;  $t(176) = 3.23, p = .001$ ) and not for individuals with higher levels of love withdrawal (placebo:  $N = 40, M = 1.15, SD = 0.47$ , oxytocin:  $N = 52, M = 1.16, SD = 0.45$ ;  $t(176) = -0.16, p = .873$ ; see Fig. 3). There was no significant three-way interaction between treatment, emotional expression, and love withdrawal ( $F(3.50, 609.13) = 1.44, p = .224$ , partial  $\eta^2 = .01$ ).

### 3.1.2. Distance: active approach

Oxytocin also reduced interpersonal distance when the participant actively approached the virtual person ( $F(1,174) = 4.72, p = .031$ , partial  $\eta^2 = .03$ ) and, again, the emotional expression of the virtual person had a significant effect ( $F(4.36, 758.60) = 2.37, p = .046$ , partial  $\eta^2 = .01$ ). There was no significant effect of love withdrawal ( $F(1,174) = 0.26, p = .610$ , partial  $\eta^2 = .00$ ). Neither were there significant interactions between treatment and love withdrawal ( $F(1,174) = 2.55, p = .112$ , partial  $\eta^2 = .01$ ), emotional expression and treatment ( $F(4.36, 758.60) = 1.34, p = .250$ , partial  $\eta^2 = .01$ ) or a significant three-way interaction between treatment, emotional expression, and love withdrawal ( $F(4.36, 758.60) = 1.14, p = .338$ , partial  $\eta^2 = .01$ ).

### 3.1.3. Anxiety: passive approach

The repeated measures ANOVA with anxiety as dependent variable showed that oxytocin did not significantly affect anxiety when the participant was approached by the virtual person ( $F(1,173) = 1.03, p = .416$ , partial  $\eta^2 = .00$ ). The main effect of love withdrawal on anxiety was not significant ( $F(1,173) = 0.40, p = .530$ , partial  $\eta^2 = .00$ ), but there was a significant effect of emotional expression on anxiety ( $F(4.17, 720.82) = 3.48, p = .004$ , partial  $\eta^2 = .02$ ), with highest anxiety in the anger condition and lowest anxiety in the happy and neutral condition (see Table 2). In addition, there was a marginally significant interaction between love withdrawal and emotional expression ( $F(4.17, 720.82) = 2.01, p = .088$ , partial  $\eta^2 = .01$ ). Individuals with higher levels of love withdrawal reported higher levels

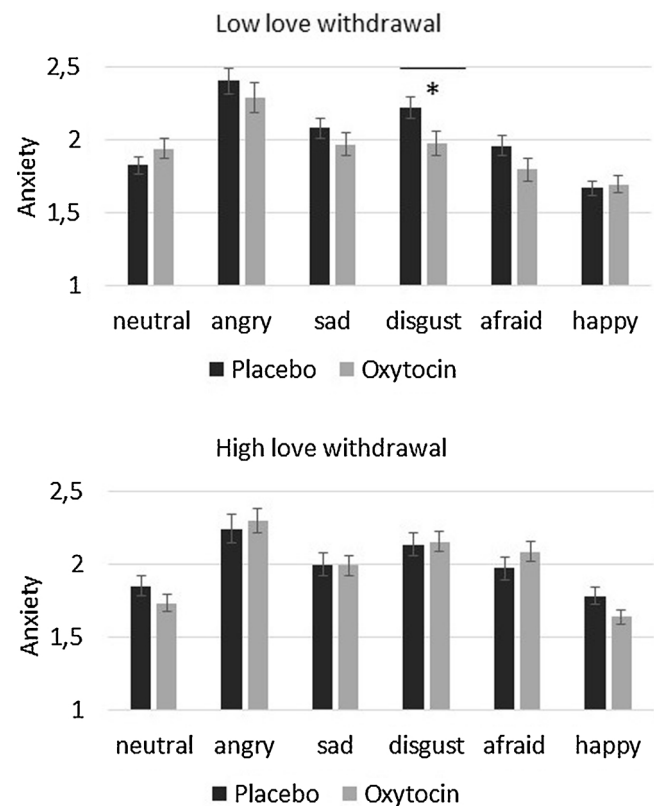


Fig. 4. Mean state anxiety (range 1–5) during the different emotion conditions for individuals with lower of higher levels of love withdrawal in the oxytocin or placebo group. \*  $p < .05$ .

of anxiety while interacting with the virtual person displaying disgust ( $F(1,173) = 3.98, p = .048$ , partial  $\eta^2 = .02$ ) and fear ( $F(1,173) = 10.81, p = .001$ , partial  $\eta^2 = .06$ ), compared to individuals with lower levels of love withdrawal. In addition, there was a significant interaction between treatment group and emotional expression ( $F(4.17, 720.82) = 2.82, p = .023$ , partial  $\eta^2 = .02$ ) and a significant three-way interaction between treatment group, emotional expression, and love withdrawal ( $F(4.17, 720.82) = 2.88, p = .020$ , partial  $\eta^2 = .02$ ). Fig. 4 presents the mean anxiety ratings across the emotion conditions for individuals in the oxytocin and placebo group with lower and higher levels of love withdrawal. Oxytocin particularly reduced anxiety levels in the disgust condition, but only for individuals with lower levels of love withdrawal. To summarize these findings, individuals with higher levels of love withdrawal tended to experience more anxiety during negatively-valenced interactions (disgust and fear, although effect size was small), but benefitted less from anxiety-reducing effects of oxytocin.

### 3.1.4. Anxiety: active approach

The repeated measures ANOVA with anxiety in the condition in which the participant actively approached the virtual person also showed a significant effect of emotional expression ( $F(3.13, 542.09) = 9.76, p < .001$ , partial  $\eta^2 = .05$ ), but no significant effect of treatment ( $F(1,173) = 2.08, p = .151$ , partial  $\eta^2 = .01$ ), love withdrawal ( $F(1,173) = 0.02, p = .900$ , partial  $\eta^2 = .00$ ), no significant interactions between treatment and emotional expression ( $F(3.13, 542.09) = 1.07, p = .364$ , partial  $\eta^2 = .01$ ), treatment and love withdrawal ( $F(1,173) = 0.93, p = .337$ , partial  $\eta^2 = .01$ ), or between treatment, emotional expression, love withdrawal ( $F(3.13, 542.09) = 0.99, p = .400$ , partial  $\eta^2 = .01$ ).

#### 4. Discussion

The aim of the current study was to examine intranasal oxytocin effects on interpersonal distance using the VR paradigm by Steenbakkers et al. (2019), in which participants were instructed to either approach a virtual person or to stop an approaching virtual person at their preferred distance. Our study extends previous research examining oxytocin effects on social approach behaviors by testing oxytocin effects on social interactions in an optimally controlled, dynamically changing virtual real life setting and by inducing different emotional facial expressions. We found that oxytocin reduced interpersonal distance during active and passive approach. In addition, oxytocin reduced anxiety, particularly while being approached by a person displaying disgust, possibly because this emotion elicited feelings of rejection.

However, oxytocin effects on distance were only present in women with low maternal disciplinary use of love withdrawal indicating a more positive family background. Moreover, women with higher levels of maternal disciplinary love withdrawal experienced more anxiety during negatively-valenced interactions, but benefitted less from anxiety-reducing effects of oxytocin.

Together, these findings do not support the social salience hypothesis. In contrast to what would be expected based on the social salience hypothesis, oxytocin did not lead to opposing effects during positively and negatively-valenced interactions. Instead, it reduced interpersonal distance in social contexts signalling threat (disgust, anger, fear) as well as safety (happy, sadness). Moreover, oxytocin did not influence the emotion ratings of the facial expressions of the virtual person, indicating that it did not affect the salience of the emotional expressions. Our results are more in line with the approach/withdrawal hypothesis. Oxytocin stimulated approach behaviors in positively-valenced interactions and reduced anxiety and withdrawal behaviors in negatively-valenced interactions, although the effects were dependent on individual characteristics.

Which possible mechanisms may underlie reduced interpersonal distance after oxytocin administration? One suggestion is that the stress-reducing and anxiolytic effects of oxytocin account for increased approach behaviors and reduced withdrawal behaviors (Piva and Chang, 2018). Multiple studies have shown that oxytocin reduces cortisol levels and stress, for example during and after psychosocial stress (Heinrichs et al., 2003). These stress reductions may in turn facilitate social approach behaviors during positive social interactions and reduce withdrawal behaviors under potentially threatening conditions. In line with this explanation, we found that oxytocin reduced anxiety during the interpersonal distance paradigm. Interestingly, anxiety-reducing effects of oxytocin were only present when participants were approached by a person displaying disgust, but no effects were found during interactions with the angry or anxious virtual person. Disgust can be interpreted as a strong social threat signalling rejection and has been shown to be more threatening to socially anxious individuals than angry faces (Amir et al., 2010). More pronounced anxiety-reducing effects of oxytocin during interactions with a disgusted person may therefore indicate that oxytocin particularly reduces social anxiety or fear of rejection. Another mechanism underlying increased approach behavior after oxytocin administration is that oxytocin may enhance the rewarding value of social interactions (Piva and Chang, 2018), in particular during positive social interactions. This hypothesis could not be tested in the current study, as we only measured state anxiety during the interpersonal distance paradigm.

Interestingly, anxiety-reducing effects of oxytocin during interactions signalling potential social threat were more pronounced for individuals with lower levels of love withdrawal than for individuals with higher levels of love withdrawal. Oxytocin also reduced interpersonal distance only for individuals with lower levels of love withdrawal, but not for individuals with higher levels of love withdrawal. This is consistent with previous studies showing less pronounced oxytocin effects

in individuals with negative childhood experiences (Meinlschmidt and Heim, 2007; Riem, Bakermans-Kranenburg, et al., 2013; Riem et al., 2013a,b). It has been suggested that epigenetic changes after childhood adversity result in reductions in oxytocin receptor expression and, as a result, influence sensitivity to intranasal oxytocin (Bakermans-Kranenburg and Van IJzendoorn, 2017). Another explanation for a reduced response to intranasal oxytocin after adverse childhood experiences is that adversity results in neuronal loss in stress-sensitive brain regions that contain high densities of oxytocin receptors (Riem et al., 2019), such as the hippocampus (Quintana et al., 2017). These neurobiological dysregulations after childhood adversity may in turn impede the feedforward mechanism of the oxytocinergic system (Churchland and Winkelman, 2012; Van IJzendoorn et al., 2012), with increased oxytocin levels after administration propagating production and release of endogenous oxytocin. This disrupted feedforward mechanism may result in more short-lived oxytocin effects or even the absence of an effect in individuals with a history of adversity. Future studies should test whether a disrupted feedforward mechanism may indeed underlie altered sensitivity to oxytocin administration in these individuals.

Another explanation for the less pronounced oxytocin effects in individuals with a history of love withdrawal is that these individuals perceived the emotional expressions of the virtual person differently. Intranasal oxytocin might not enhance prosocial behavior in individuals with more love withdrawal because these experiences may have resulted in an insecure internal working model (Bowlby, 1969), which may alter the interpretation of social stimuli (Zik and Robert, 2015). Indeed, our results showed that individuals with experiences of love withdrawal rated the angry virtual person as less angry, possibly because of attentional disengagement. A previous study showed that love withdrawal is associated with enhanced early attention to and processing of facial stimuli as indicators of the relational consequences linked to failure and success, but diminished attentional engagement at a later processing stage (Huffmeijer et al., 2013). This pattern of early vigilance and later avoidance has been suggested to explain attentional biases to threat and disturbed emotional face processing in maltreated individuals (Hein and Monk, 2017; Masten et al., 2008). One possibility is that attentional disengagement may have resulted in reduced attention to social threat cues and may thus have interfered with anxiety-reducing effects of oxytocin in individuals with higher levels of love withdrawal. However, this explanation may be less likely as self-reported anxiety levels were particularly high when these individuals were approached by a person displaying negative emotions. Thus, even though individuals with love withdrawal seemed to perceive the angry virtual person as less threatening, they tended to experience more anxiety while being approached by a virtual person than individuals with a positive family background and benefitted less from oxytocin.

It should be noted that, although the majority of previous studies indicates that intranasal oxytocin effects are hindered in individuals with a history of negative caregiving experiences, two studies show an opposite pattern, with more prosocial effects of oxytocin after childhood adversity. Riem et al. (2014) showed that intranasal oxytocin enhances emotion recognition, as measured with the Reading the Mind in the Eyes Test (RMET, Baron-Cohen et al., 1997), particularly in individuals who reported higher levels of maternal use love withdrawal. Similarly, Schwaiger et al. (2019) showed improved performance on the RMET after oxytocin administration in individuals with a history of adversity, but not in individuals without adverse experiences. Oxytocin may particularly improve emotion recognition in individuals with adversity, because negative parenting experiences increase the risk for developing poor theory of mind skills (Cicchetti et al., 2003). Indeed, research shows that oxytocin effects are a function of the baseline socio-emotional abilities, with stronger effects for individuals who fail to interpret social cues at baseline (Luminet et al., 2011). Together, this pattern of findings seems to indicate that the moderating influence of caregiving experiences on the effects of oxytocin may depend on the outcome that is at stake. Whereas anxiolytic effects and effects on social

behavior seem to be hindered in individuals with a history of adversity, improvements in socio-cognitive functioning after intranasal oxytocin may be preserved.

An interesting finding of the current study is that oxytocin affected state anxiety during the interpersonal distance paradigm, but the direction of the effects was dependent on experiences of love withdrawal and the emotional expression of the virtual person. This indicates that the effect of oxytocin was shaped by an individual difference *and* social context factor and adds to many previous studies pointing to a variety of social contexts and individual difference moderators of the effects of oxytocin (Bartz et al., 2011; Shamay-Tsoory and Abu-Akel, 2016). Moreover, our study extends previous studies by *simultaneously* examining both contextual and individual difference moderators, which is important because these moderators are likely interrelated. More specifically, the way one perceives a certain stimulus or social context (e.g., what constitutes a cue of social threat) may depend on the personal relevance of that social stimulus. Indeed, Harari-Dahan and Bernstein (2017) recently showed that oxytocin effects are modulated by the degree to which social or non-social stimuli have motivational relevance. They found that, rather than enhancing the salience of social stimuli per se, oxytocin stimulates approach behaviors only when the stimuli are emotionally evocative and motivationally relevant for the participant. Future studies should therefore simultaneously examine both individual difference and context factors.

Examining both individual difference and contextual factors will offer a better integrated framework for the role of oxytocin in social behavior and decision making, which is needed to advance understanding of oxytocin's therapeutic potential for clinical groups. Our finding that oxytocin reduced anxiety during personal space intrusion is consistent with prior studies showing anxiolytic oxytocin effects during social stress (e.g. Heinrichs et al., 2003) and may have clinical implications. For example, there is increasing interest for potential therapeutic use of oxytocin for the treatment of psychopathologies associated with anxiety and social dysfunctions, such as generalized anxiety disorder or posttraumatic stress disorder (Neumann and Slattery, 2016). However, clinical trials examining oxytocin effects in psychiatric groups have shown disappointing results so far, with mixed effects (Guastella et al., 2015, 2009). Meta-analyses examining beneficial oxytocin effects in clinical groups show that effects are inconclusive (De Cagna et al., 2019; Keech et al., 2018) or are limited to psychiatric conditions with etiological factors unrelated to childhood adversity (e.g. autism; Bakermans-Kranenburg and Van IJzendoorn, 2013). Thus, there is no strong evidence that oxytocin may be an effective pharmacological intervention for reducing general psychiatric symptoms. However, the majority of clinical trials so far have neglected the role of individual differences in sensitivity to intranasal oxytocin and the role of social context. Given the evidence for a dysregulated oxytocin system after childhood adversity, future clinical studies should therefore take into account the role of childhood trauma and examine whether oxytocin may be effective for specific diagnostic subgroups without trauma. Moreover, future studies should examine how negative childhood experiences result in a dysregulated oxytocin system and investigate whether individuals with trauma do benefit from repeated intranasal oxytocin or different dosages and/or in different stages of the therapeutic process.

Some limitations should be noted. First, although the ratings of the emotional expressions of the virtual person showed that the emotions were all correctly recognized, the emotional expressions may have differed in the clarity by which the emotion was expressed. For example, the angry facial expressions and gestures of the virtual person may be easier to recognize than the expressions and gestures of the happy virtual person. Second, we cannot rule out influences of pre-existing differences between the oxytocin and placebo group because of the use of a between-subject design, although randomization has reduced this risk. Another limitation is the use of a short retrospective self-report questionnaire to assess childhood experiences. In addition,

only the relationship with mother was assessed. Interviews assessing the quality of relationship of both parents might yield more valid data. Lastly, the findings of the current study can only be generalized to women without children.

## 5. Conclusions

Using the innovative, immersive VR paradigm by Steenbakkers et al. (2019) we examined oxytocin effects on interpersonal distance in a dynamically changing, but optimally controlled real life setting. This study is the first to investigate how contextual and individual characteristics in *tandem* modulate the effects of oxytocin on prosocial behavior in VR. We found that oxytocin reduced interpersonal distance between a participant and a virtual person with various emotional expressions. Oxytocin effects on approach behavior were particularly pronounced in individuals with lower levels of (disciplinary) maternal love withdrawal, but absent in individuals with higher levels of love withdrawal. Moreover, women with higher levels of maternal disciplinary love withdrawal experienced more anxiety while being approached by a virtual person than individuals with a more positive family background regarding this aspect, but benefitted less from oxytocin. This is consistent with previous research showing a dysregulated oxytocinergic system after childhood adversity and may indicate that oxytocin may be less effective for individuals who are most in need of an intervention because of a problematic family background.

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## Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.psyneuen.2019.06.012>.

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